

Disclosures.

### **Rejection Under 35 U.S.C. § 101**

Claim 24 was rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. Claim 24 has been canceled herein. This rejection has been rendered moot.

### **Rejections Under 35 U.S.C. § 112, first paragraph**

Claims 22 and 24 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. Claims 22 and 24 have been canceled herein. This rejection has been rendered moot.

### **Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 1-21 were rejected as allegedly indefinite regarding the intended use of the vector because. Claim 1 has been amended to recite that the vector is intended for expressing a gene of interest in a "host cell of specific tissue type", thereby covering *in vivo* and *in vitro* use. Support for this amendment can be found, *inter alia*, on page 7, lines 7 through 15, of the application as filed. Applicants respectfully request that this rejection be withdrawn.

Claims 1-21 were rejected as allegedly indefinite in the recitation of the phrase "gene of interest." Applicants respectfully traverse this rejection. It is clear that the claims encompass any gene of interest. "Gene of interest" is defined on pages 23-24 of the application as filed as comprising therapeutically useful nucleic acid sequences. Numerous examples of therapeutically useful nucleic acid sequences are provided therein. Applicants respectfully request that this rejection be withdrawn.

Claims 5, 14, and 16 were rejected as allegedly indefinite in view of the recitation "consisting essentially of." Claims 5, 14, and 16 as amended herein no longer recite the objectionable phrase. This rejection has been obviated by amendment. Applicants respectfully request that this rejection be withdrawn.

Claims 12-21 were rejected as allegedly indefinite. The Examiner stated that it was unclear whether the replication protein was necessary for one or both origins of replication and, further, whether the origins of replication are the same. Claim 12 has been amended herein to clarify that the origins of replication are the same. Applicants respectfully request that this

rejection be withdrawn.

Claim 25 was rejected as allegedly indefinite in its recitation of "the LCR or component thereof which is only active in the cell line in which the LCR when integrated is active." The Examiner stated that the meaning of the phrase cannot be deciphered. Applicants respectfully traverse this rejection.

Claim 25 is directed to identifying LCRs and components of LCRs which direct expression of a gene in a tissue-restricted manner when comprised in an episome. To identify such LCRs and LCR components, one transfets cell lines in which the LCR is otherwise known to be active when integrated as well as cell lines in which the LCR is otherwise known to be inactive when integrated, i.e., in other than an episome. If the LCR or LCR component comprised in an episome is only active in the cell lines in which the LCR or LCR component is known to be active, then tissue-restricted expression has been maintained. Nonetheless, in an effort to advance prosecution, Applicants have amended claim 25 to clarify that the identification is of the *episomally-contained* LCR or LCR component that is claimed. Applicants respectfully request that this rejection be withdrawn.

#### **Rejection Under 35 U.S.C. § 103(a)**

Claims 1-3, 5-14, and 16-21 were rejected as allegedly unpatentable over Yates et al., Sadelain et al., Greaves et al., Grosveld et al., Ustav et al., and Svensson et al.

The Examiner admits, however, that none of the references cited teach the use of a LCR in self-replicating vectors. Indeed, the Examiner failed to establish the motivation to modify the references to yield Applicants' invention. Rather than establishing motivation, the Examiner argued simply that, "since it would have been desirable to achieve tissue specific expression using episomal vectors, one would have been motivated to incorporate LCR sequences into episomes . . ." But the Examiner has not cited to any reference stating that it would have been desirable to achieve tissue specific expression using episomal vectors. If the Examiner is relying upon her own personal knowledge, Applicants request an affidavit pursuant to 37 C.F.R. § 1.104(d)(2) or a withdrawal of this rejection. Additionally, the Examiner appears to be relying upon the virtues of Applicants' invention to support her rejection for obviousness (see page 11 of

the Office Action). This is a clear use of inappropriate hindsight. Applicants respectfully request that this rejection be withdrawn.

Claim 23 was rejected as allegedly unpatentable over the references cited above as applied to claims 1-3, 5-14, and 16-21, further in view of Chapman et al. Applicants respectfully traverse this rejection.

The deficiencies of the references cited for claims 1-3, 5-14, and 16-21 are discussed above, discussion incorporated herein. Chapman et al. does not overcome these deficiencies. Chapman et al. is relied upon for the transfection of cultured cells. Chapman et al., however, does not disclose or suggest the use of an LCR in an episomal vector. Applicants request that this rejection be withdrawn.

Claim 25 was rejected as allegedly unpatentable over the references cited for claim 23. Applicants respectfully traverse this rejection.

The deficiencies of the references cited for claims 1-3, 5-14, and 16-21 are discussed above, discussion incorporated herein. Chapman et al. does not overcome these deficiencies. Chapman et al. is relied upon for disclosing the effect of intron A from human cytomegalovirus immediate early gene on heterologous expression in mammalian cells. Chapman et al., however, does not even suggest testing candidate regulatory elements, much less LCRs. The Examiner made a giant leap from Chapman et al. to finding testing candidate LCR sequences as claimed obvious. Applicants respectfully request that this rejection be withdrawn.

Applicants reserve the right to respond to the remaining references cited by the Examiner on PTO-892 at such time that they are relied upon.

For the foregoing reasons, the Applicants submit that the present description and claims

meet all the requirements for patentability. The Examiner is respectfully requested to allow all the present claims.

Respectfully submitted

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